

Translational Research Working Group

Envisioning the Future of NCI's Investment in Translational Research

Roundtable II

October 16 & 17, 2006

Atlanta, Georgia



NATIONAL INSTITUTES OF HEALTH

Ernest Hawk, MD, MPH
National Cancer Institute
Office of Centers, Training & Resources



TRWG Co-Chairs

Lynn Matrisian, PhD

- Ingram Distinguished Professor of Cancer Research
 - Professor & Chair, Department of Cancer Biology
 - Vanderbilt-Ingram Comprehensive Cancer Center

William G. Nelson, IV, MD, PhD

- Associate Director, Translational Research
- Professor of Oncology, Urology, Pharmacology, Medicine & Pathology
- Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

TRWG Roundtable II - Goals

- To share the TRWG's products to date
 - TR Definition
 - Process analysis – 20 case studies
 - Portfolio analysis – current status of NCI's investments
 - Pathways to clinical goals – 5 developmental algorithms
 - Draft initiatives
- To receive broad, substantive input into draft initiatives
- To solicit recommendations regarding implementation

Perspectives on Translational Research

- **Developmental Pathways or Product Lines**
 - Pharmacologic interventions
 - Immunologic interventions
 - Interventive devices
 - Risk assessment devices
 - Image-based
 - Molecular/biomarker-based
 - Lifestyle recommendations
- **Cross-cutting Themes**
 - Solicitation, review, funding
 - Prioritization
 - Interactions
- Management
- Facilities/technologies
- Commercialization
- Workforce/training
- **Populations Intended to Benefit**
 - Organ-based
 - “Rare” tumors
 - Minority/underserved
 - Pediatric
- **Clinical Intentions**
 - Risk reduction/prevention
 - Early-disease therapy
 - Late-disease therapy
 - Palliation

General Handout Materials

- Agenda
- Roster of attendees
- Draft initiatives
 - Coordinated management
 - Tailored funding mechanisms
 - Operational effectiveness
- Developmental pathways to clinical goals
- Process analysis summary
- Portfolio analysis summary
- TR definition
- Background
 - Funding mechanism definitions
 - Public comment synthesis
 - Roundtable I executive summary
 - ONC study section descriptors
 - NCI program summaries

TRWG Roundtable II Agenda

8:00-9:30 am

Introduction

- *TRWG Scope/Definition of Translational Research*
- *Review Pathways*
- *Process Analysis*
- *Portfolio Analysis*
- *TR Issues – Public Comment & Roundtable I*

9:30-10:00 am

Break

10:00-11:30 am

Recommended Initiatives

- *Goals*
- *Implementation Concepts*

Objectives for Current Roundtable

11:30-Noon

Lunch

TRWG Roundtable II Agenda

Noon-2:00 pm Breakout Session 1 – Coordinated Management

- Agents – Therapy*
- Agents - Prevention*
- Immune Response Modifiers – Therapy/Prevention*
- Risk Assessment Devices – Molecular Markers*
- Interventive Devices/Risk Assessment Devices – Imaging*
- Lifestyle Alterations*
- Pediatrics/Rare Cancers*
- Minority/underserved Populations*

2:00-3:00 pm Break

3:00-4:30 pm Moderated Report-out Session

TRWG Roundtable II Agenda

5:00-7:00 pm

Breakout Session 2 – Tailored Funding Mechanisms

- Agents – Therapy*
- Agents - Prevention*
- Immune Response Modifiers – Rx/Prev*
- Risk Assessment Devices – Molecular Markers*
- Interventive Devices/Risk Assessment Devices – Imaging*
- Lifestyle Alterations*
- Pediatrics/Rare Cancers*
- Minority/underserved Populations*

7:00 pm

Adjournment

----- TUESDAY, OCTOBER 17, 2006 -----

8:00-10:00 am

Moderated Report-out Session

10:00-10:30 am

Break

TRWG Roundtable II Agenda

10:30-Noon Breakout Session 3 – Operational Effectiveness

- Project Management*
- Core Services Coordination*
- Annotated Biospecimen Repositories*
- Intellectual Property*
- Integration with Industry*
- Integration with Foundations/Advocacy Groups*
- Workforce/Training*

Noon-1:00 pm Lunch

1:00-3:00 pm Individual Report-out Session

3:00-4:00 pm Wrap-up & Next Steps

4:00 pm Adjournment

Contacts During the Roundtable Meeting

- **Scientific goals & content**

- Ernie Hawk
- Lynn Matrisian
- Bill Nelson
- Judy Hautala
- Lisa Stevens
- Jaye Viner

- **Logistical issues**

- Facilitators & scientific writers
- Janet Braun or Dana Young of NOVA Research
 - Accommodations
 - Travel
 - Messages
 - Services

Foundational Principles

- Structure serves function
- TRWG members are serving as
 - Team members
 - Content experts
 - Component leaders
 - Ambassadors
- The TRWG has & will continue serving as a model for all that we're trying to achieve on a larger scale

Acknowledgements

- National Cancer Institute
 - Anna Barker, PhD
 - Jim Doroshow, MD
 - Maureen Johnson, PhD
 - Jennifer Kwok
 - Anne Lubenow
 - Cherie Nichols, MBA
 - John Niederhuber, MD
 - Lisa Stevens, PhD
 - Jaye Viner, MD, MPH
- Science & Technology Policy Institute
 - Oren Grad, MD, PhD
 - Judy Hautala, PhD
 - Maureen McArthur
 - Alexis Wilson
 - Brian Zuckerman, PhD
- Science Applications International Corp.
 - Jeff Zalatoris, PhD
- NOVA Research
 - Janet Braun
 - Erin Milliken
 - Dana Young
- Vanderbilt University
 - Lynn Matrisian, PhD
- Johns Hopkins University
 - Bill Nelson, MD, PhD

NIH Mission Statement

“Science in pursuit of fundamental knowledge about the nature and behavior of living systems

&

the application of that knowledge to extend healthy life and reduce the burdens of illness and disability”

<http://www.nih.gov/about/index.html#mission.htm>

Medicine's Emerging Transformation

Transition will be fueled by translational science

20th Century	21st Century	Implications
Treat disease when symptoms appear & normal function is lost	Intervene before symptoms appear & preserve normal function for as long as possible	Prevention of disease & health preservation
Cross-sectional, morphologic definition & understanding of disease	Dynamic, cellular/molecular understanding of disease processes	Prediction of risk earlier & better; more effective, less toxic interventions
Expensive in financial & disability costs	Improved opportunities for effectiveness & efficiency	Personalization of risks & interventions

Adapted from presentations by L Hood, A von Eschenbach & E Zerhouni, 2005-2006

Forces Affecting Translational Progress

“Suppressors”

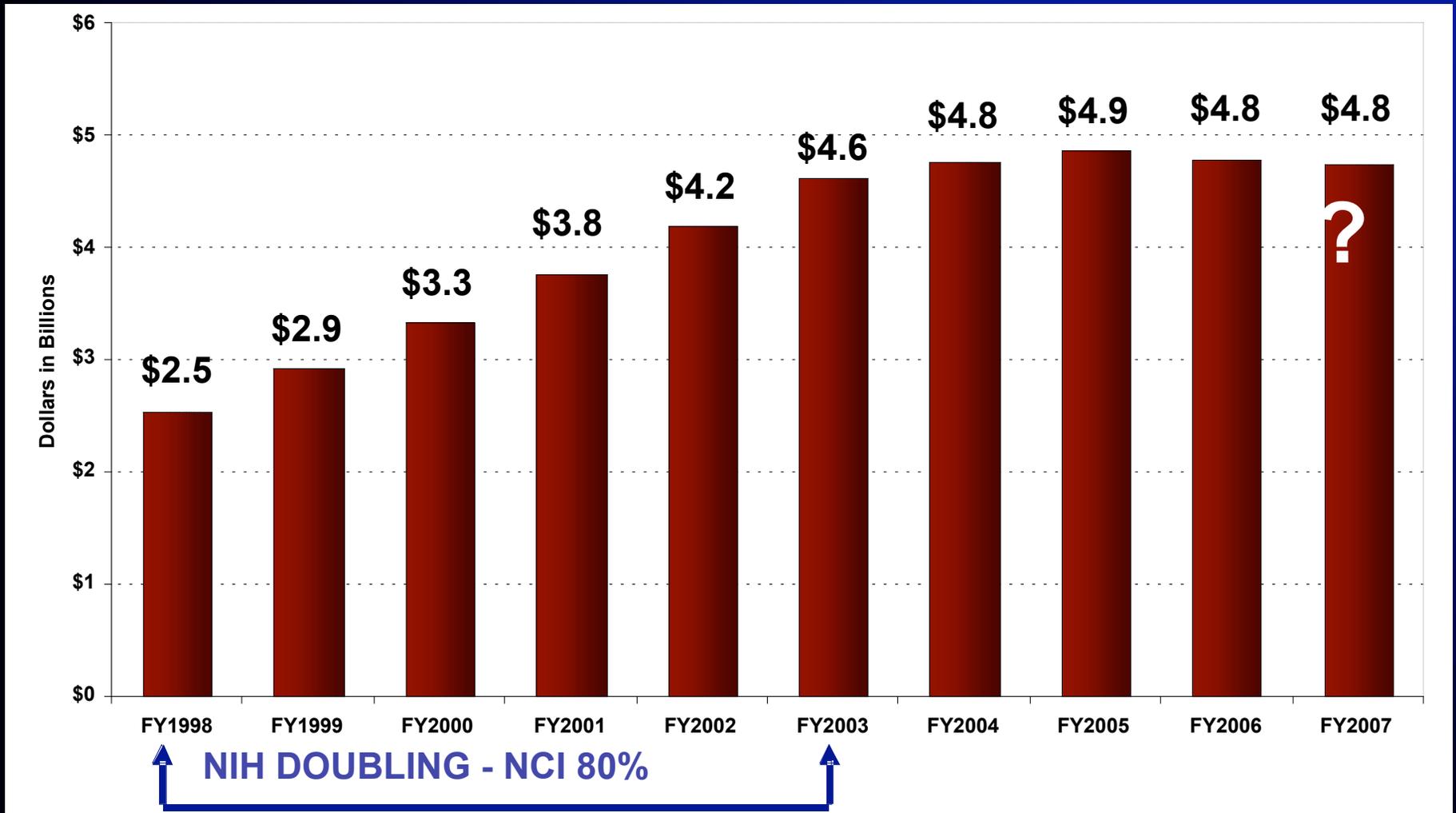
- **Behavioral inertia**
 - Diet
 - Exercise
 - Chemical abuse
 - Tobacco
 - Alcohol
 - Drugs
- **Aging**
- **Resource limitations**
 - Time
 - Money
 - Personnel
- **Disorganization**
 - Cacophony vs. symphony
- **Narrow focus**

“Activators”

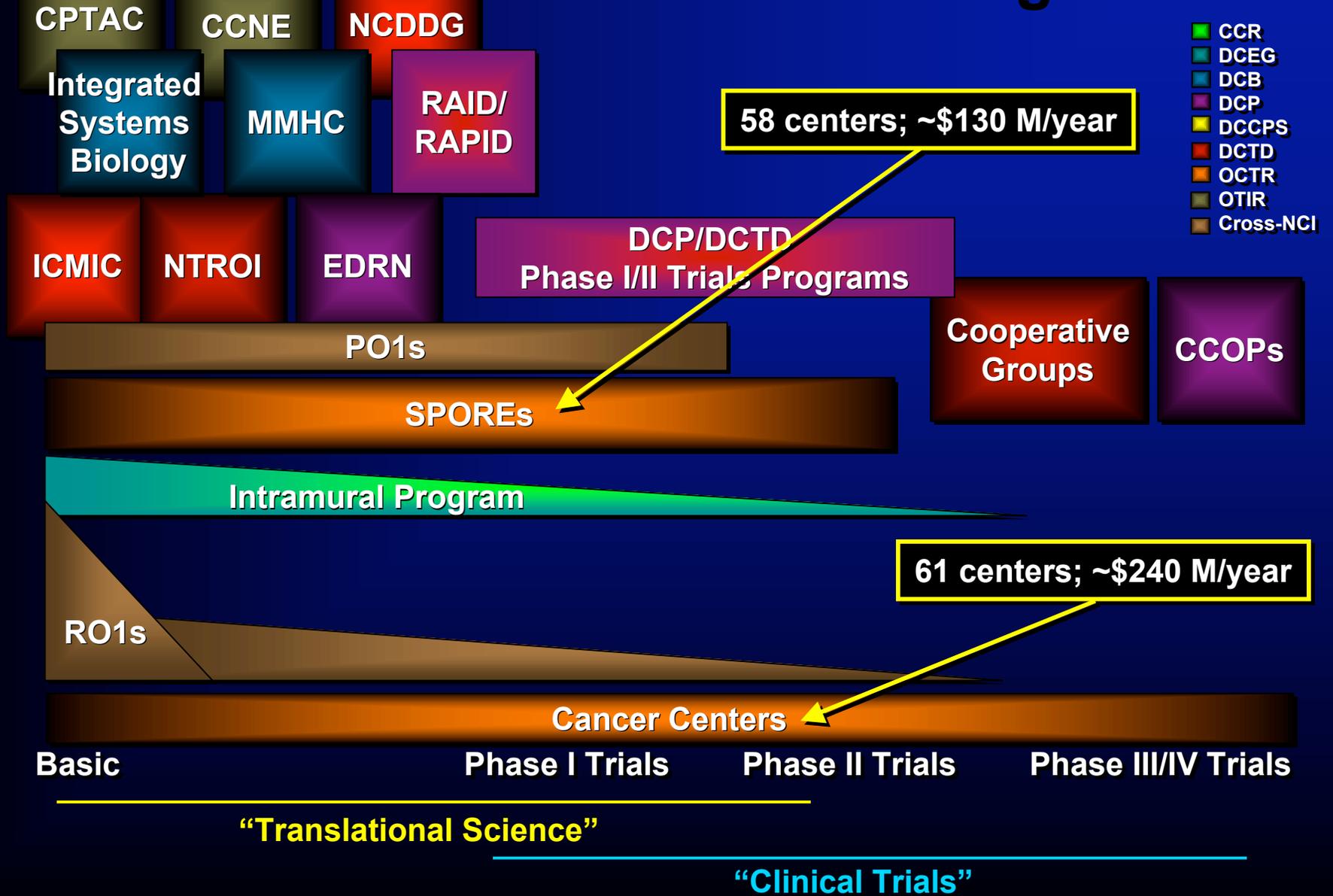
- **Molecular insights**
 - “-omics”
 - Targeted therapies
 - Biotherapies (e.g., vaccines)
- **Shared aberrancies underlying diverse diseases of aging**
- **Advances in imaging**
 - Virtual, serial exams
 - Noninvasive, molecular insights
- **Communication**
 - E-records
 - Standardized tools (e.g., ca-BIG)
- **Partnerships**

NCI's Congressional Appropriation

FY 1998 - FY 2007

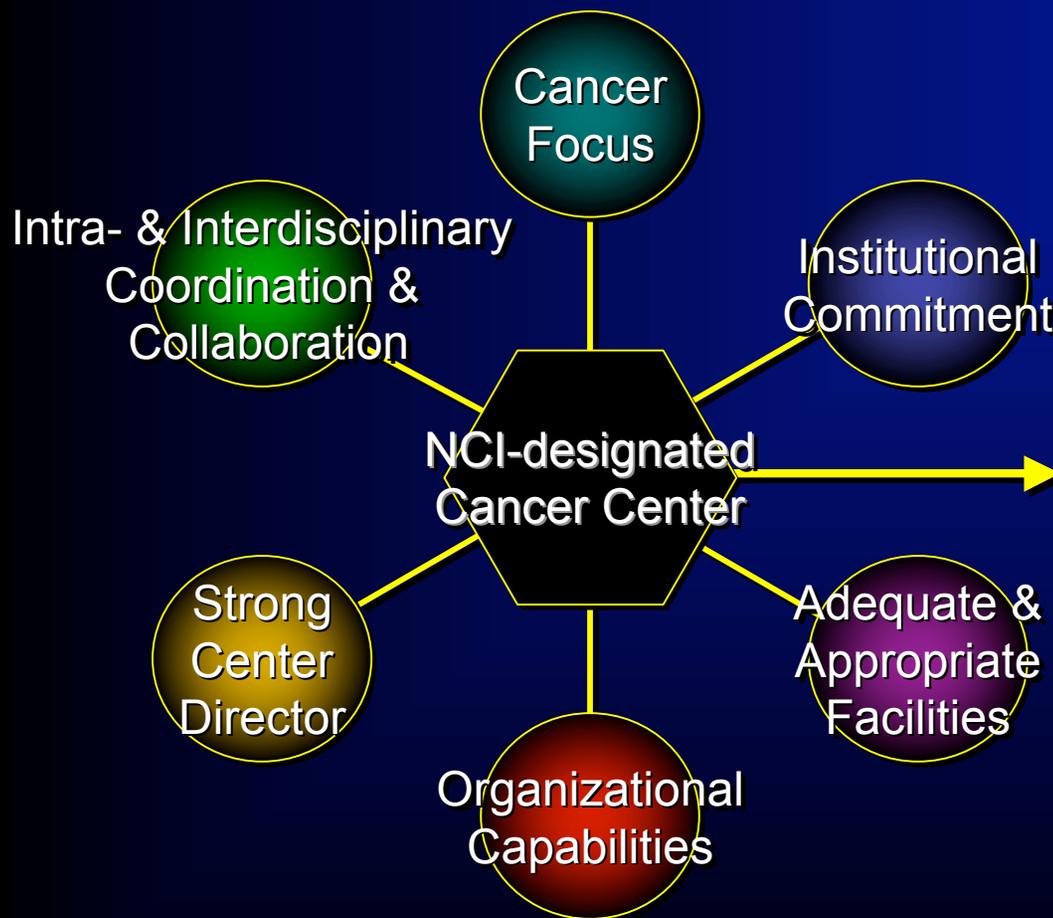


NCI's "Bench to Bedside & Back" Research Infrastructure & Programs



NCI-Designated Cancer Centers – Characteristics & Components

Has/receives



Provides

- Administration
- Senior Leadership
- Staff Investigators
- Planning & Evaluation
- Scientific Programs
- Shared Resources
 - Biostatistics, informatics, etc.
- Protocol Review & Monitoring System
- Protocol-specific Research Support
- Data & Safety Monitoring
- Data Sharing
- Developmental Funds
 - Pilot projects, recruitment, new shared resources, new technologies/methodologies, interim support

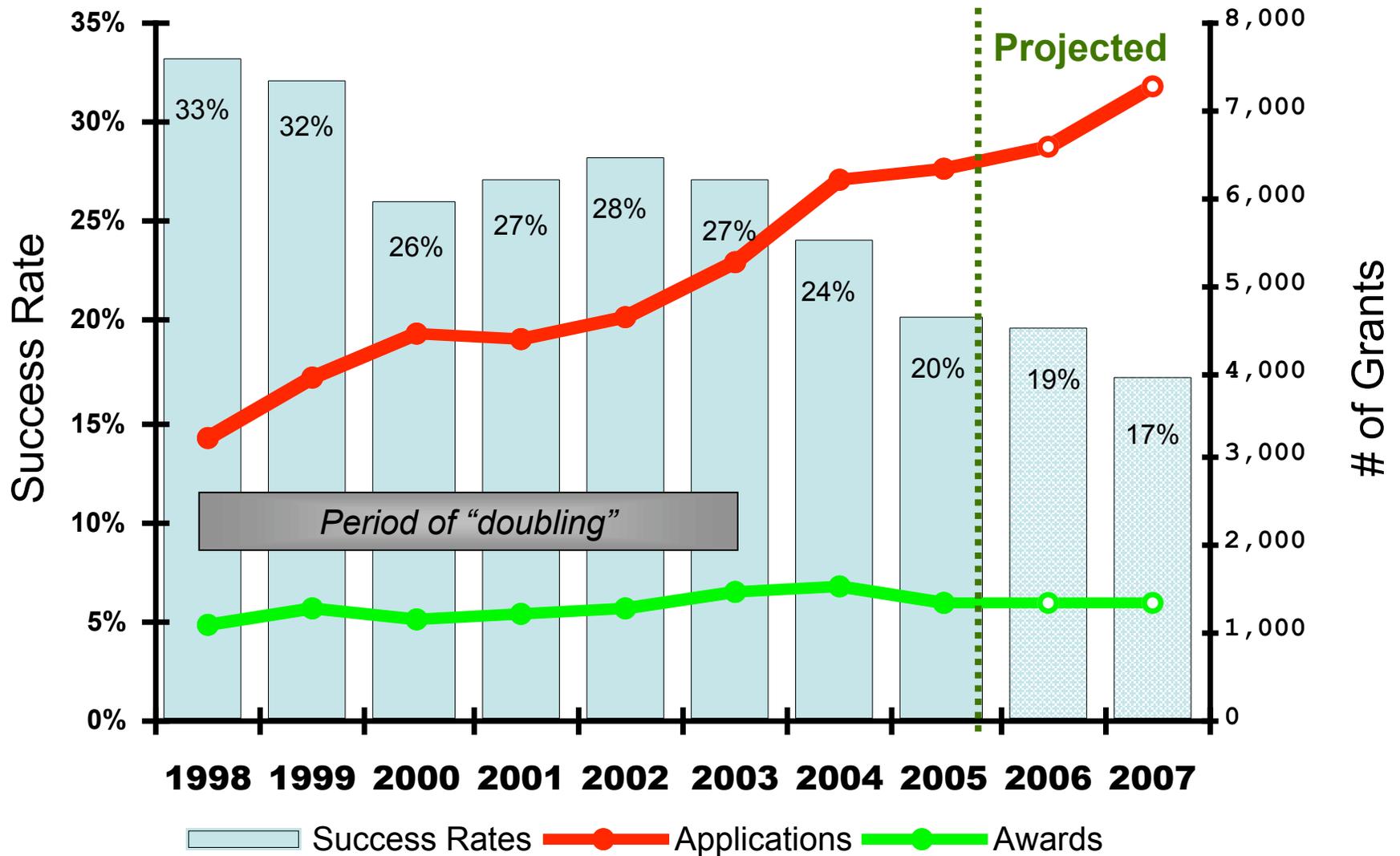
President's NCI Budget Proposal for FY07 vs. FY06

FY06 Appropriation	\$4,793,356
FY07 President's Budget	\$4,753,609
Difference '06 to '07	- \$39,747
Percent Change '06 to '07	- 0.8%

(dollars in thousands)

NCI Applications, Awards & Success Rates

1998 to 2007 Estimates of Competing RPGs



What is Driving NCI's Budget Situation?

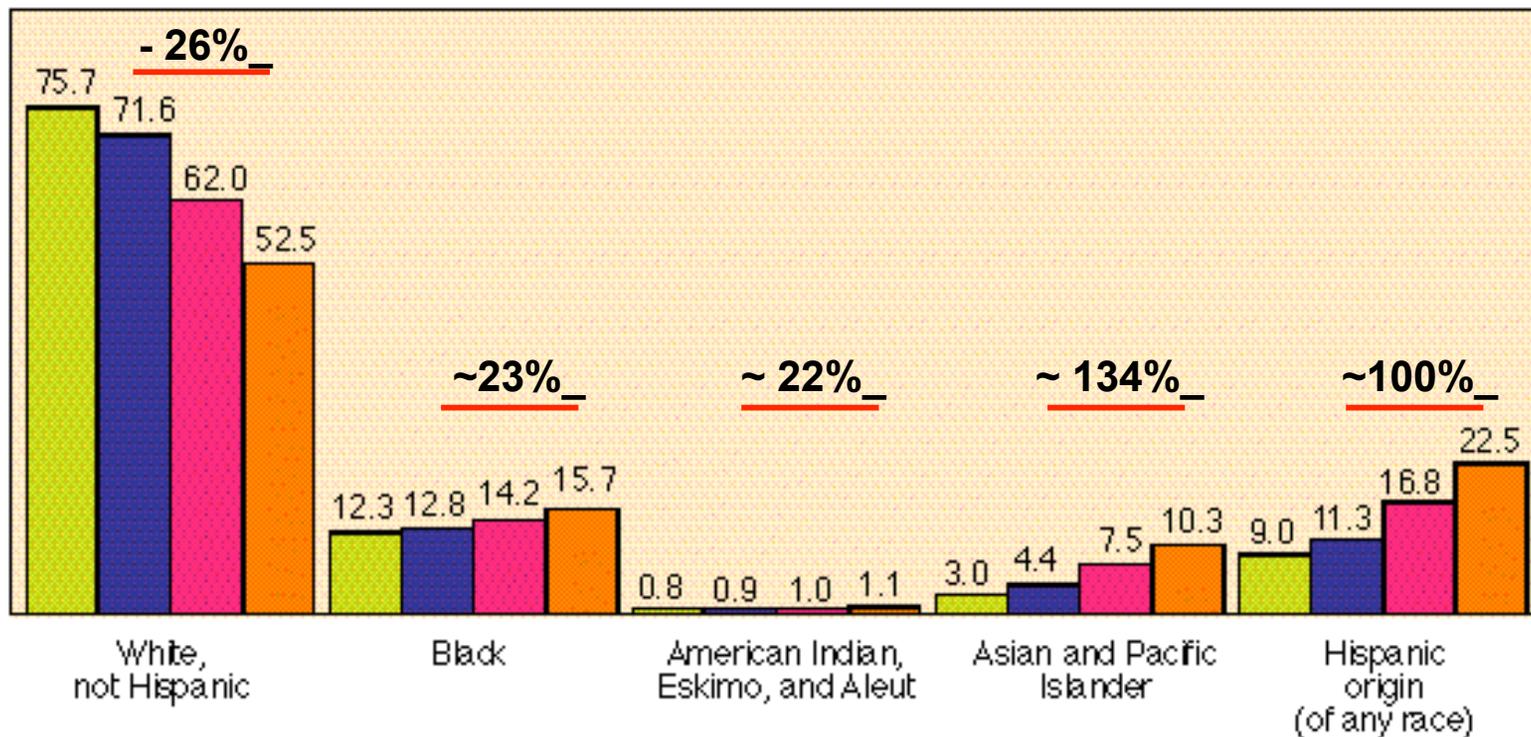
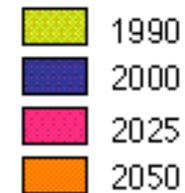
- **Unanticipated expenditures**
 - Defense & Homeland Security (-2.7% for HHS)
 - Disasters/disaster planning (Katrina, pandemic flu)
- **Misperception**
 - “Budget doubling” should have been sufficient to fuel immediate clinical improvements
- **Missed opportunity**
 - Cancer research rarely viewed as a key to advancing public health & national prosperity
- **Increased capacity**
 - More competitive institutions & researchers
- **Biomedical research inflation of ~ 4%**

U.S. Population - Growing More Diverse

(highlighting relative changes between 2000 and 2050)

Percent of the Population, by Race and Hispanic Origin: 1990, 2000, 2025, and 2050

(Middle-series projections)



Source: U.S. Census Bureau, Population Division and Housing & Household Economic Statistics Division; Last Revised: January 18, 2001
<http://www.census.gov/population/www/pop-profile/natproj.html>

NIH Roadmap

New Pathways to Discovery

**Research Teams
of the Future**



**Re-engineering the
Clinical Research
Enterprise**

New Clinical & Translational Science Awards

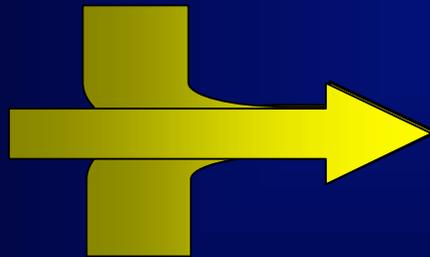
- Columbia University Health Sciences (*New York, N.Y.*)
- Duke University (*Durham N.C.*)
- Mayo Clinic College of Medicine (*Rochester, Minn.*)
- Oregon Health & Science University (*Portland, Ore.*)
- Rockefeller University (*New York, N.Y.*)
- University of California, Davis (*Davis, Calif.*)
- University of California, San Francisco (*San Francisco, Calif.*)
- University of Pennsylvania (*Philadelphia, Pa.*)
- University of Pittsburgh (*Pittsburgh, Pa.*)
- University of Rochester (*Rochester, N.Y.*)
- University of Texas Health Science Center at Houston (*Houston, Texas*)
- Yale University (*New Haven, Conn.*)

Why Convene a TRWG? Why Now?

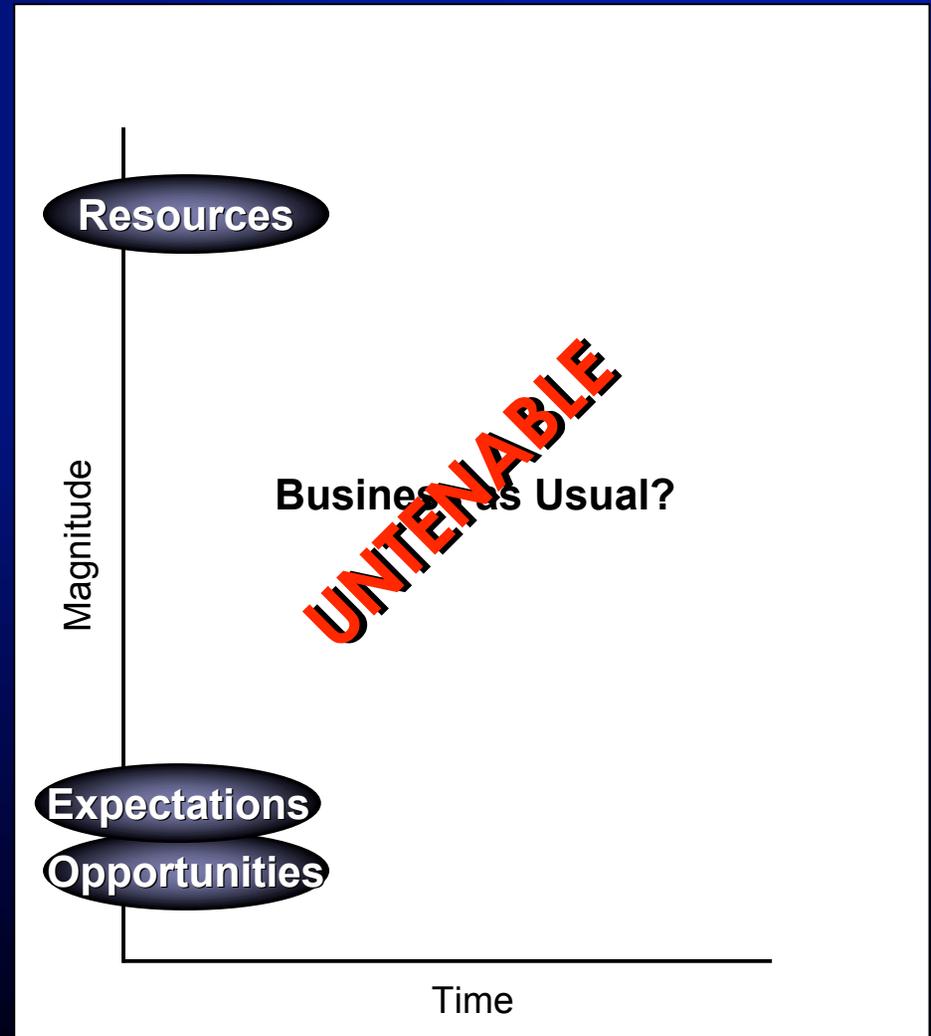
Major advances in cancer biology

Changing environment

- Growth
- Diversity
- Competition



Translational systems that cannot keep pace



Translational Research Working Group

Charge:

Evaluate the current status of NCI's investment in translational research & envision its future in an inclusive, representative & transparent manner

TRWG Membership

Abbruzzese, James	Dubinett, Steven	Limburg, Paul	Perez-Soler, Roman
Alberts, David	DuBois, Raymond	Look, A. Thomas	Rabkin, Charles
Anderson, Kenneth	Emanuel, Peter	Lubenow, Anne	Reid, Brian
Bast, Robert	Esserman, Laura	Lyerly, H. Kim	Scheinberg, David
Bigner, Darell	Fenton, Laurie	Maslow, David	Schilsky, Richard
Buetow, Kenneth	Gilmer, Tona	Matrisian, Lynn	Schlom, Jeffrey
Caligiuri, Michael	Gomez, Jorge	McGrath, Gail	Schnall, Mitchell
Cheever, Martin	Gordon, Gary	McLeod, Howard	Sellers, Thomas
Collins, Jerry	Gray, Joe	McTiernan, Anne	Sidransky, David
Cote, Richard	Gritz, Ellen	Mohla, Suresh	Sigal, Ellen
Courtneidge, Sara	Hait, William	Moore, Ida "Ki"	Simon, Richard
Cowan, Kenneth	Hawk, Ernest	Nelson, William	Srivastava, Sudhir
Dennis, Phillip	Hong, Waun Ki	Nichols, Cherie	Sullivan, Daniel
Di Bisceglie, Adrian	Jacks, Tyler	Olopade, Olufunmilayo	Tlsty, Thea
Doroshov, James	Kerr, David	Oberholtzer, John Carl	Weiner, Louis
Downing, Gregory	Lawrence, Theodore	Pazdur, Richard	

Programmatic Representation on the TRWG

(CRISP Database, 2000-2006)

- **Cancer Centers (8)**

- David Alberts
- Michael Caligiuri
- Kenneth Cowan
- Raymond Dubois
- Peter Emanuel
- William Hait
- Tyler Jacks
- H. Kim Lyerly

- **Industry (4)**

- Martin Cheever
- Sara Courtneidge
- Tona Gilmer
- Gary Gordon

- **EDRN (2)**

- David Sidransky
- Sudhir Srivastava

- **Advocates (3)**

- Laurie Fenton
- Gail McGrath
- Ellen Sigal

- **SPOREs (14)**

- James Abbruzzese
- Kenneth Anderson
- Robert Bast
- Darell Bigner
- Richard Cote
- Steven Dubinett
- Laura Esserman
- Joe Gray
- Waun Ki Hong
- Lynn Matrisian
- William Nelson
- Olufunmilayo Olopade
- David Sidransky
- Thea Tlsty

- **Clinical Study Consortia (5)**

- David Alberts
- Michael Caligiuri
- James Doroshow
- Paul Limburg
- Richard Schilsky

- **P01s (18)**

- David Alberts
- Kenneth Anderson
- Robert Bast
- Michael Caligiuri
- Richard Cote
- Steven Dubinett
- Raymond Dubois
- Gary Gordon
- Joe Gray
- Waun Ki Hong
- Tyler Jacks
- Theodore Lawrence
- A. Thomas Look
- H. Kim Lyerly
- Brian Reid
- David Scheinberg
- Mitchell Schnall
- Thomas Sellers

Programmatic Representation on the TRWG

(CRISP Database, 2000-2006)

- **R01s (30)**
 - Kenneth Anderson
 - Robert Bast
 - Michael Caligiuri
 - Martin Cheever
 - Richard Cote
 - Sara Courtneidge
 - Adrian DiBisceglie
 - James Doroshow
 - Steven Dubinett
 - Raymond Dubois
 - Peter Emanuel
 - Ellen Gritz
 - William Hait
 - Theodore Lawrence
 - Paul Limburg
 - A. Thomas Look
 - H. Kim Lyerly
 - Lynn Matrisian
 - Anne McTiernan
 - Ida “Ki” Moore
 - William Nelson
 - John Carl Oberholtzer
- **R01s (cont.)**
 - Olufunmilayo Olopade
 - Roman Perez-Soler
 - Brian Reid
 - David Scheinberg
 - Thomas Sellers
 - David Sidransky
 - Thea Tlsty
 - Louis Weiner
- **Training/Education (15)**
 - David Alberts (R25, T32)
 - Robert Bast (K12, T32)
 - Michael Caligiuri (T32)
 - James Doroshow (K12)
 - Raymond Dubois (T32)
 - Peter Emanuel (T32)
 - Waun Ki Hong (T32)
 - H. Kim Lyerly (K12, T32)
 - Lynn Matrisian (T32)
 - Ida “Ki” Moore (T32)
 - Olufunmilayo Olopade (T32)
 - David Scheinberg (K12)
 - Mitchell Schnall (T32)
- **Training/Ed (cont.)**
 - Thomas Sellers (R25)
 - Louis Weiner (K12)
- **Federal Gov’t (17)**
 - Kenneth Buetow (CB)
 - Jerry Collins (DCTD)
 - Phillip Dennis (CCR)
 - James Doroshow (DCTD)
 - Gregory Downing (OTIR)
 - Jorge Gomez (OCTR)
 - Ernest Hawk (OCTR)
 - Anne Lubenow (OC)
 - David Maslow (DEA)
 - Suresh Mohla (DCB)
 - Cherie Nichols (OSPA)
 - John Carl Oberholtzer (OCTR)
 - Richard Pazdur (FDA)
 - Charles Rabkin (DCEG)
 - Jeffrey Schlom (CCR)
 - Richard Simon (DCTD)
 - Sudhir Srivastava (DCP)
 - Daniel Sullivan (DCTD)

TRWG Expertise in Various Populations

- **Head & Neck**
 - Waun Ki Hong
 - David Sidransky
- **Lung**
 - Phillip Dennis
 - Steven Dubinett
 - Laurie Fenton
 - Waun Ki Hong
 - Roman Perez-Soler
- **Stomach/Esophagus**
 - Ernest Hawk
 - Paul Limburg
 - Brian Reid
- **Pancreas**
 - James Abbruzzese
- **Liver**
 - Adrian DiBisceglie
 - Theodore Lawrence
 - Charles Rabkin
- **Colorectum**
 - James Doroshow
 - Raymond Dubois
 - Ernest Hawk
 - Paul Limburg
 - Richard Pazdur
 - Jeffrey Schlom
- **Breast**
 - Kenneth Cowan
 - Laura Esserman
 - Joe Gray
 - William Hait
 - H. Kim Lyerly
 - Anne McTiernan
 - Olufunmilayo Olopade
 - Mitchell Schnall
 - Thomas Sellers
 - Thea Tlsty
- **Ovary/Gyn**
 - David Alberts
 - Robert Bast
 - Thomas Sellers
- **GU**
 - Richard Cote
- **Prostate**
 - William Nelson
- **Brain**
 - Darrel Bigner
- **Skin**
 - David Alberts
- **Leukemia/Lymphoma**
 - Michael Caligiuri
 - Peter Emanuel
 - A. Thomas Look
 - David Scheinberg
- **Myeloma**
 - Kenneth Anderson

TRWG Expertise in Special Scientific Areas

- **Prevention**
 - David Alberts
 - Adrian DiBisceglie
 - Steven Dubinett
 - Raymond Dubois
 - Laura Esserman
 - Gary Gordon
 - Ellen Gritz
 - Ernest Hawk
 - Waun Ki Hong
 - Paul Limburg
 - Lynn Matrisian
 - Anne McTiernan
 - William Nelson
 - Olufunmilayo Olopade
 - Charles Rabkin
 - Brian Reid
 - Thomas Sellers
 - David Sidransky
 - Sudhir Srivastava
 - Thea Tlsty
- **Pediatrics**
 - Peter Emanuel
 - A. Thomas Look
- **Survivorship**
 - Ida “Ki” Moore
- **Genetics**
 - Kenneth Buetow
 - Joe Gray
 - Olufunmilayo Olopade
 - William Nelson
 - Charles Rabkin
 - Thomas Sellers
 - David Sidransky
- **Imaging**
 - Daniel Sullivan
 - Mitchell Schnall
- **Drugs/Immunologics**
 - James Abbruzzese
 - David Alberts
 - Kenneth Anderson
 - Martin Cheever
 - Jerry Collins
 - Michael Caligiuri
 - Sara Courtneidge
 - Kenneth Cowan
 - James Doroshow
 - Tona Gilmer
- **Drugs/Immunologics (cont.)**
 - Gary Gordon
 - William Hait
 - Ernest Hawk
 - Waun Ki Hong
 - Paul Limburg
 - H. Kim Lyerly
 - William Nelson
 - Richard Pazdur
 - Roman Perez-Soler
 - David Scheinberg
 - Jeffrey Schlom
 - Richard Schilsky
 - Ellen Sigal
 - Richard Simon
 - Louis Weiner
- **Biobehavior**
 - Ellen Gritz
 - Anne McTiernan
- **Preclinical Models**
 - Tyler Jacks
 - Lynn Matrisian
 - Suresh Mohla
 - Thea Tlsty

TRWG Strategic Plan

1. Acknowledge prior/concurrent efforts

- CTWG report
- P30/50 Working Group
- PRG reports
- FDA's Critical Path initiative
- President's Cancer Panel
- NIH Roadmap initiatives
- NCAB report (*Cancer at a Crossroads*)

2. Define scope of activity

3. Map & evaluate existing programs

- Portfolio analysis
- Process analysis

4. Provide vision & recommendations

- Near-term adjustments of existing programs
- Long-term vision transcending existing programs

5. Develop implementation strategy

TRWG Progress to Date

- Recruited TRWG leadership & members
- Reviewed foundational documents
- Analyzed Clinical Trials Working Group process for ideas, challenges & lessons learned
- Developed web-based communication platform
- Gathered public input on key questions
 - Web-based system
 - Roundtable I
- Analyzed NCI's current investments in TR
 - Portfolio analysis
 - Process analysis
- Mapped 5 developmental pathways to clinical goals
- Constituted 6 subcommittees
 - Organization & funding
 - Core services
 - Training/workforce
 - Prioritization
 - Project management
 - External integration

TRWG's Web-based Communication Platform

A Critical Link to the Wider Community

- <http://www.cancer.gov/trwg>
- Information on the TRWG process, leaders, & members
- Used for the public comment sessions
 - First public comment period
 - December 20, 2005 - January 27, 2006
 - Second public comment period
 - October 13, 2006 – November 3, 2006
- Other venues for facilitated outreach
 - Teleconferences
 - Advocacy organizations, ASCO
 - Meetings
 - SPORE, EDRN, NCAB, BSA, Industry/foundation RT

Public Comment - I

- “Questions” subcommittee
 - Jim Abbruzzese
 - Ken Anderson
 - Laurie Fenton
 - Anne Lubenow
- 20 questions on 8 broad topics
 - Definition
 - Barriers/incentives
 - Prioritization
 - Funding
 - System organization
 - Facilities/technologies
 - Manpower/training
 - “Other issues”
- Public comment web-link
 - December 20, 2005 – January 27, 2006

Respondents

Demographics	Total	Percentage of Responses
Academic - translational	46	25.7
Patient advocate/patient	33	18.4
Academic – clinical	19	10.6
Academic – basic	17	9.5
Government	17	9.5
Other	17	9.5
Community health professional	8	4.5
Industry	8	4.5
Care provider	5	2.8
General public	4	2.2
NGO/foundation	3	1.7
Legal/regulatory	2	1.1
Total	179	100.0

TRWG Roundtable I – Phoenix, February 2006

Three Perspectives on Translational Science

- **Developmental Pathways to Clinical Goals**
 - Agents (small molecules, targeted agents)
 - Immunologics & vaccines
 - Interventive devices
 - Lifestyle alterations
 - Risk devices
- **Cross-cutting Themes**
 - Identification/solicitation
 - Review
 - Funding
 - Management approaches
 - Collaboration/cooperation/communication
 - Facilities/technologies
 - Facilitating commercialization: IP, licensing, regulatory issues
 - Workforce/training
 - Roles of industry/academia/gov't
 - Evaluation metrics
- **Populations Intended to Benefit**
 - “At risk”
 - Early/late disease
 - Minorities/underserved
 - Pediatric
 - Patients with “rare” cancers

TRWG Roundtable I Results

- ~ 375 recommendations
 - “Big picture” & specific
 - Evolutionary & revolutionary
 - Organized into 6 thematic areas
 - Resources
 - Workforce/training
 - Structure/management of overall system
 - Project selection/conduct/management
 - External integration
 - Other
 - Recommendations served as a premise for TRWG’s subcommittee structure

TRWG Industry/Foundation/Society Roundtable – Philadelphia, April 2006

8:30

Welcome & Introductions

9:00 – 1:30

Small Group Discussions

- Resources
- Pathways
- Collaborations
- Management

1:30 – 3:30

Reports from Small Groups

3:30 – 4:30

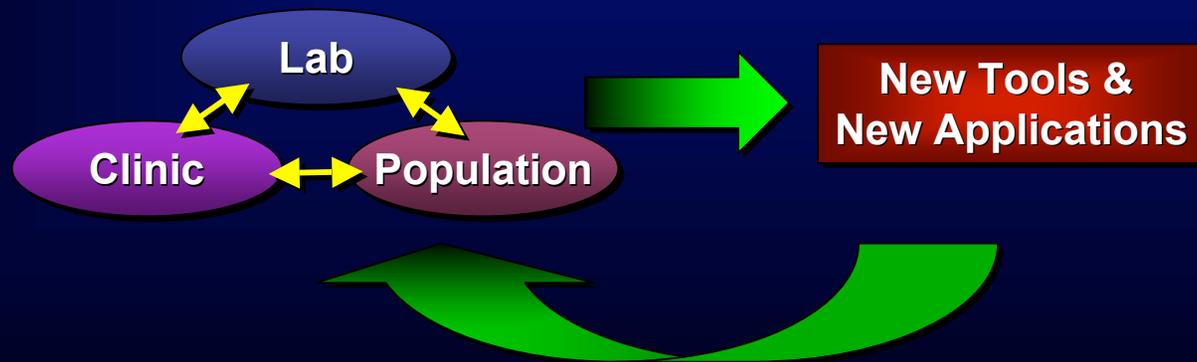
Discussion of Recommendations

TRWG Products to Date

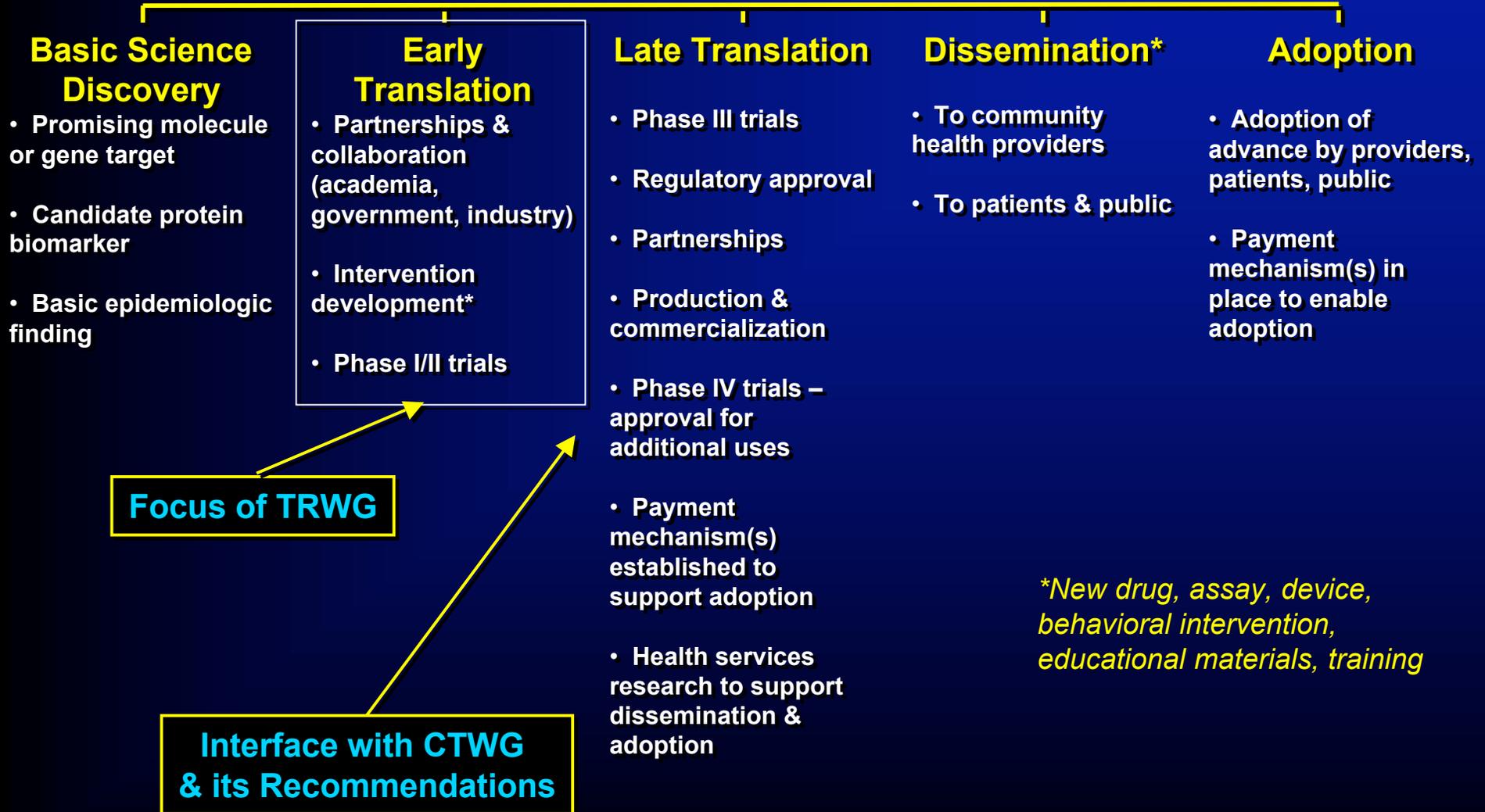
- TR definition
- Five developmental pathways to clinical goals
- Process analysis
 - Case studies of 20 examples of translation in practice
- Portfolio analysis
 - Review of NCI's current TR activities
- Seventeen draft initiatives

TRWG's Definition of Translational Research

- Research that transforms scientific discoveries arising in the lab, clinic or population into new clinical tools & applications that reduce cancer incidence, morbidity & mortality

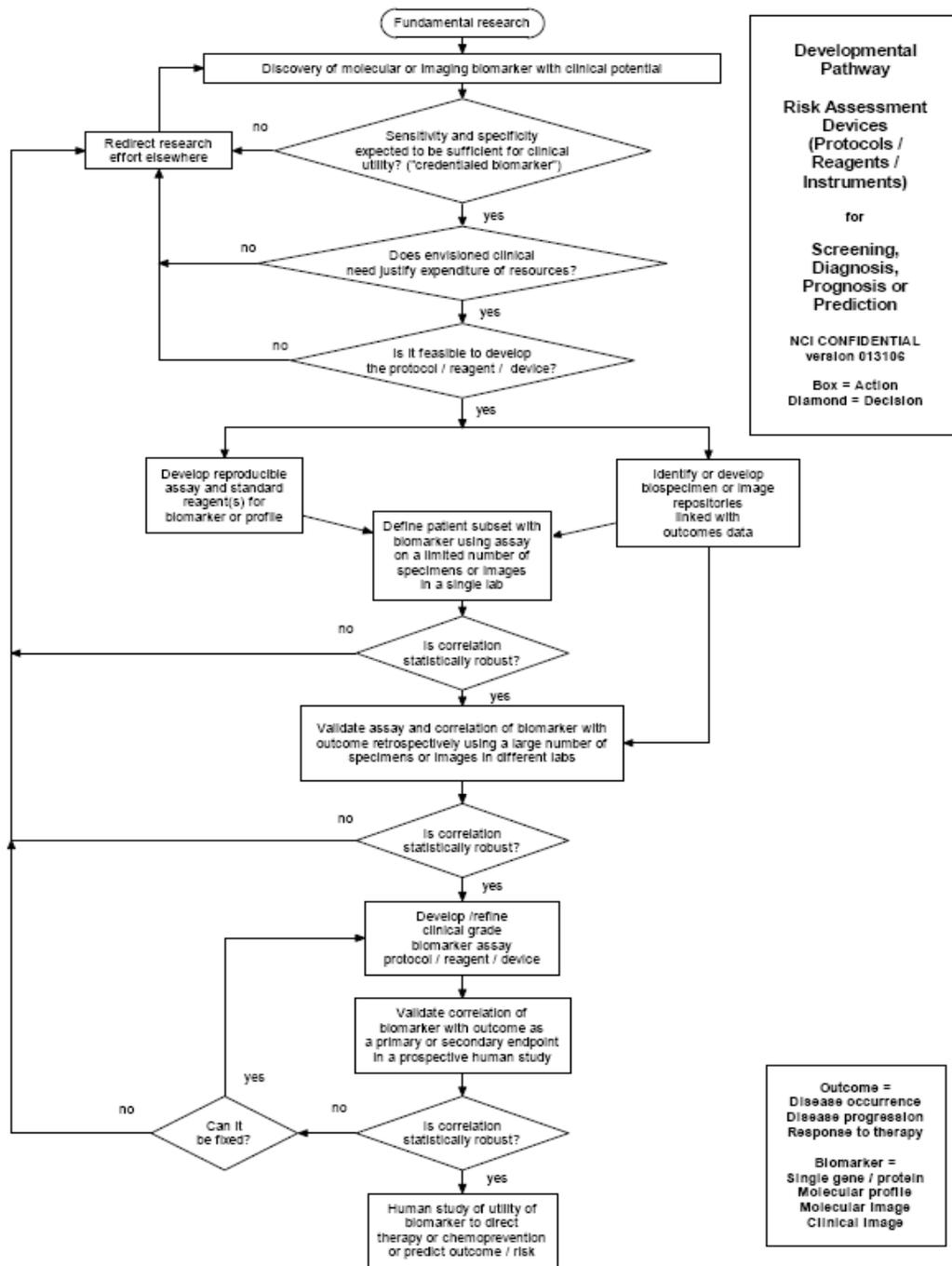


The Translational Continuum



Five Pathways to Clinical Goals

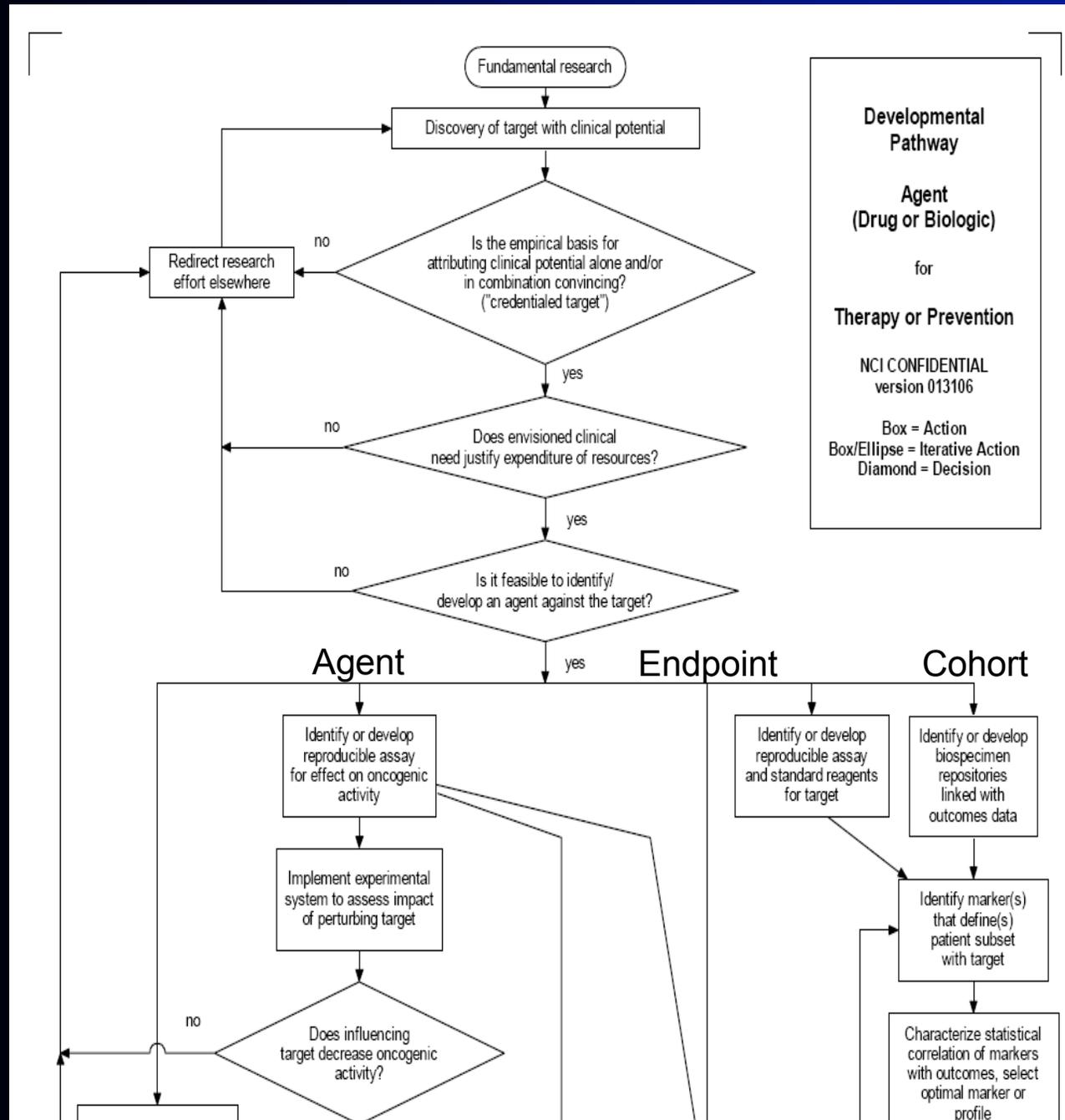
- Agent
- Immune Response Modifier
- Interventive Device
- Risk Assessment Device
- Lifestyle Alteration



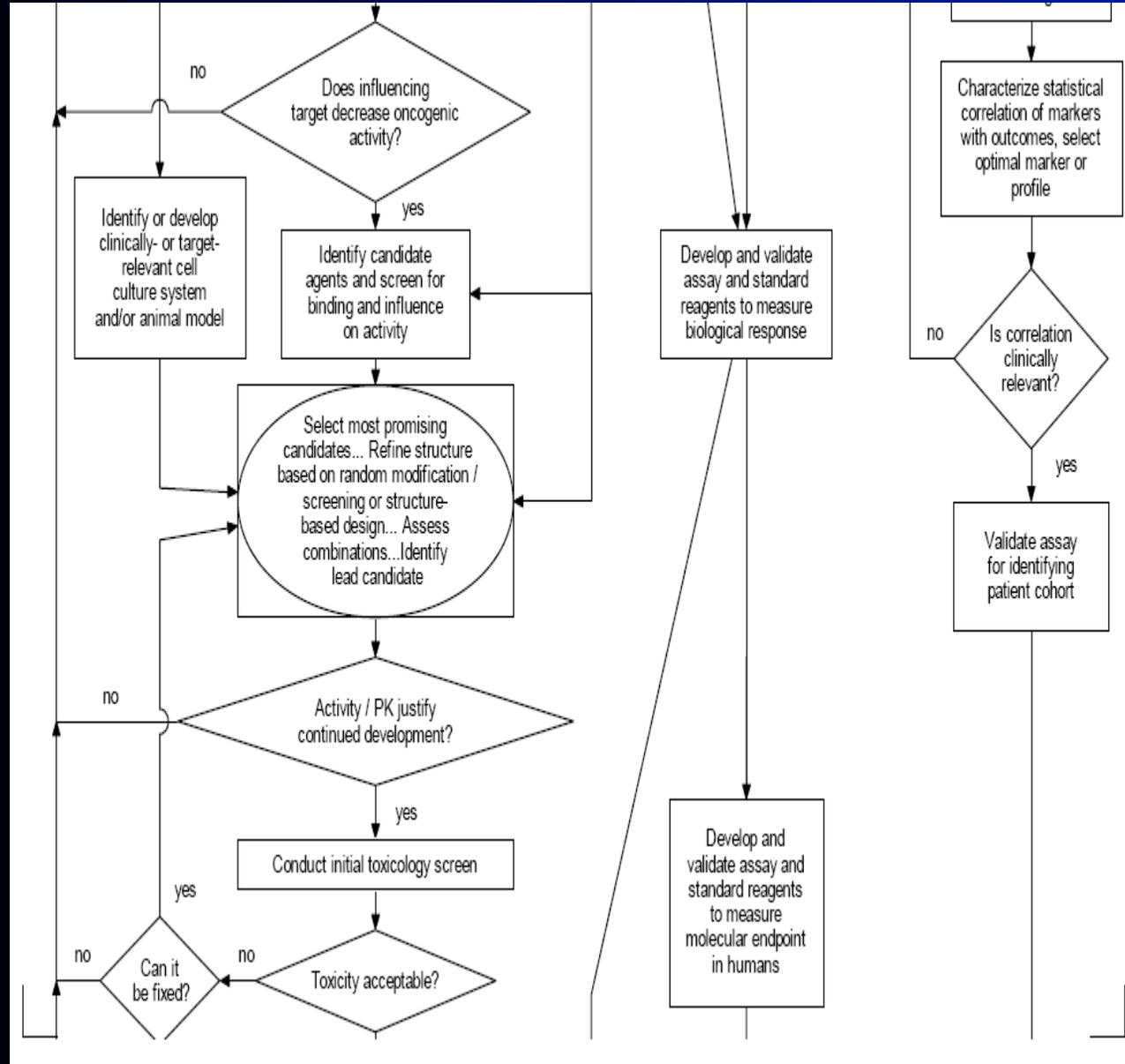
Developmental Pathway
Risk Assessment Devices
 (Protocols / Reagents / Instruments)
 for
Screening, Diagnosis, Prognosis or Prediction
 NCI CONFIDENTIAL version 013106
 Box = Action
 Diamond = Decision

Outcome =
 Disease occurrence
 Disease progression
 Response to therapy
Biomarker =
 Single gene / protein
 Molecular profile
 Molecular image
 Clinical image

Risk Assessment Devices

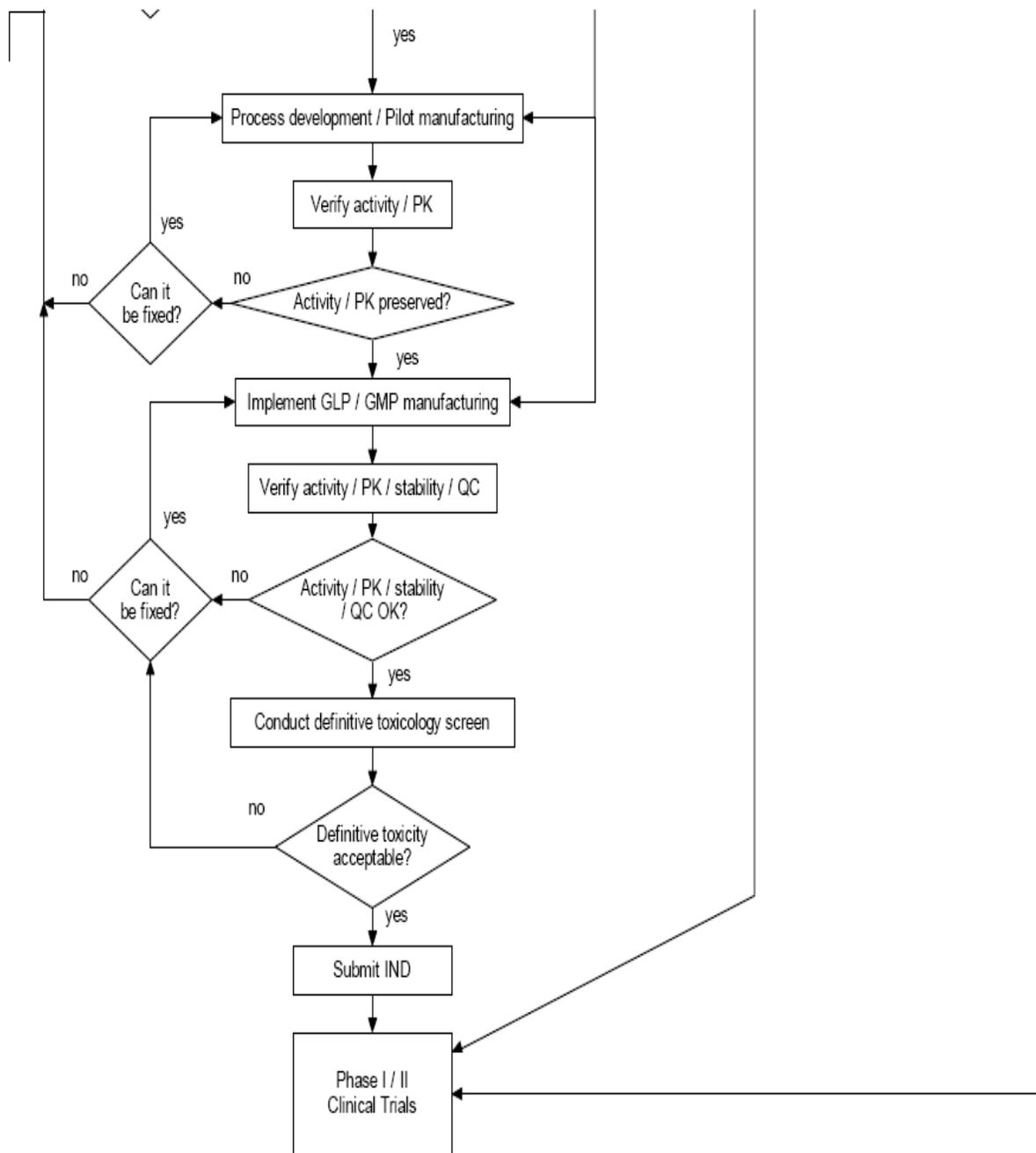


Agents – Drug or Biologic (part 1)



Agents – Drug or Biologic (part 2)

Agents – Drug or Biologic (part 3)



TRWG Process Analysis - Goals

- To systematically review a sample of NCI's translational portfolio and learn
 - Which paths translation takes?
 - How do case studies relate to the translational pathways?
 - Commonalities
 - Bottlenecks
 - What roles do academia, industry, and NCI play?
 - In our current systems & processes, what are
 - Strengths
 - Limitations
 - Interactions
 - Gaps
 - “Lessons learned”

TRWG Process Analysis - Methods

- TRWG identified ~4 case studies/pathway
- Compiled & reviewed (for each case)
 - Publications
 - Grant abstracts
 - Clinical trials abstracts
 - Other publicly-available information
- Interviewed key contributors
- Mapped cases against pathway diagrams
- Selected cases for Roundtable discussion

Process Analysis: Key Findings

- **Translation Occurs via Diverse Mechanisms**
 - Single facilitated program
 - Series of individual-investigator awards
 - NCI intramural research program
 - Combination of mechanisms
 - Mechanisms from NCI & other Institutes
- **Translation Occurs via Diverse Stakeholder Interactions**
 - Academia with industry funding
 - Traditional hand-off from academia to industry
 - Public/private partnership
 - Industry discoveries advancing with NCI-funded resources

Portfolio Analysis

- **Goals**

- Scrutinize the NCI's current TR portfolio
 - Infrastructures
 - Investigator-initiated projects
 - Facilitated programs

- Inform the TRWG regarding
 - Organization
 - Capabilities
 - Challenges/needs

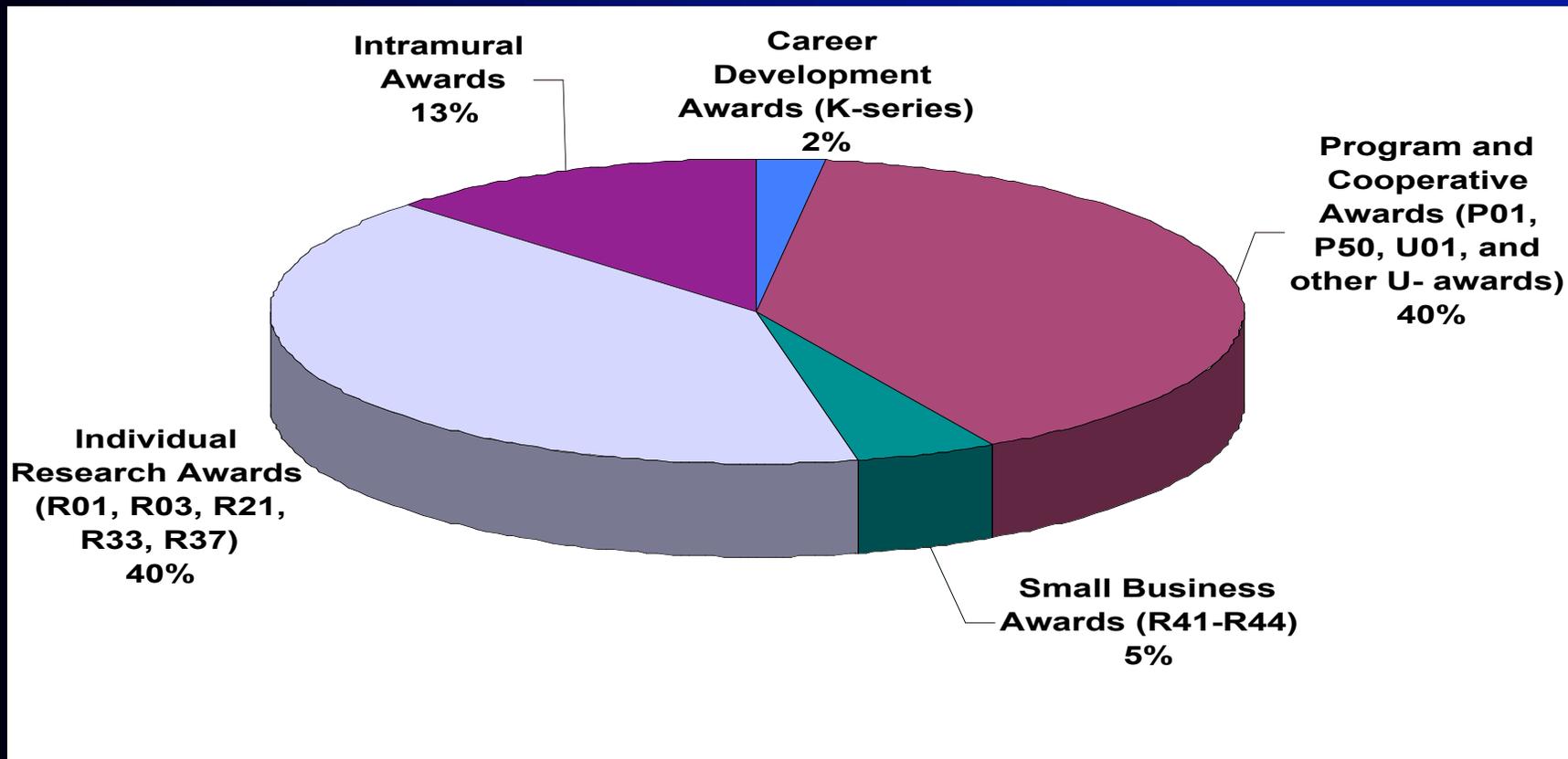
Portfolio Analysis - Methodology

- Research programs & awards active in FY04 as reflected in the Cancer Research Portfolio were compiled and assessed for their relevance to translational research
 - Use of existing coding system where possible
 - Abstract reviews when needed
 - Specific inclusion/exclusion criteria
- Evaluation
- Assessment of validity
 - Methods
 - “Positive” controls
 - “Negative” controls
 - Focus
 - Inclusion criteria
 - Research funding estimates

NCI Programmatic Involvement in Developmental Pathways

Pathway Steps Pathway	Early Development of Intervention	Enabling technologies (e.g., assays, repositories, models)	Refinement	Manufacturing/ Production	Early-stage trials
Agents (not including imaging agents)	SPORE, NCDDG, CCNE, R01, P01, Z01	MMHCC, CPTAC, SPORE, NCDDG, CCNE, R01, P01, Z01	SPORE, RAID, RAPID, NCDDG, CCNE, R01, P01, Z01	SPORE, RAID, RAPID, CCNE, R01, P01, Z01	Cancer Centers, Cooperative Groups, SPORE, DCP Phase I/II, DCTD Phase I/II, R01, P01, Z01
Immune Response Modifiers	SPORE, NCDDG, CCNE, R01, P01, Z01	MMHCC, SPORE, NCDDG, CPTAC, CCNE, R01, P01, Z01	SPORE, RAID, RAPID, NCDDG, CCNE, R01, P01, Z01	SPORE, RAID, RAPID, R01, P01, Z01	Cancer Centers, Cooperative Groups, SPORE, DCTD Phase I/II, R01, P01, Z01
Risk Assessment Devices (Biomarkers)	SPORE, EDNR, CPTAC, CCNE, R01, P01, Z01	MMHCC, EDNR, CPTAC, CCNE, R01, P01, Z01	SPORE, EDNR, CCNE, R01, P01, Z01	SPORE, CCNE, R01, P01, Z01	SPORE, EDNR, R01, P01, Z01
Risk Assessment Devices (Imaging, Imaging Agents, and Imaging Devices)	SPORE, ICMIC, NTROI, CCNE, R01, P01, Z01	MMHCC, CPTAC, ICMIC, NTROI, CCNE, R01, P01, Z01	SPORE, ICMIC, NTROI, DCIDE, CCNE, R01, P01, Z01	SPORE, ICMIC, NTROI, DCIDE, CCNE, R01, P02, Z01	Cancer Centers, CIP Quick Trials, SPORE, ICMIC, NTROI, R01, P01, Z01
Interventive Devices	SPORE, CCNE, R01, P01, Z01	MMHCC, CPTAC, SPORE, CCNE, R01, P01, Z01	SPORE, CCNE, R01, P01, Z01	SPORE, R01, P01, Z01	SPORE, Cancer Centers, Cooperative Groups, R01, P01, Z01
Lifestyle Interventions	SPORE, R01, P01, Z01	MMHCC, MMHCC, SPORE, R01, P01, Z01	SPORE, R01, P01, Z01	SPORE, R01, P01, Z01	Cancer Centers, SPORE, Cooperative Groups, R01, P01, Z01

Translational Portfolio Analysis by Funding Mechanisms Percent of NCI Budget



- Figure is based on FY2004 allocated budget of the NCI awards in this translational portfolio, \$1.3 Billion.
- Data exclude RAID (DTP), DDG (DTP), RAPID (DCP), U24 EDNRN (DCP) developmental programs, & infrastructure awards.

Portfolio Analysis: Program and Cooperative Awards

Award Category	Translational Awards	Total Active Awards	% Translational	TR Award Funding in FY04 (\$M)
P01*	107	207	51.7%	\$215.0
P20	8	34	23.5	3.0
SPORE* (P50)	58	58	100	\$131.7
ICMIC (P50)	7	7	100	15.8
EDRN (U01/U24)	28	28	100	21.8
MMHCC (U01)	10	23	43.5	8.1
Other U01	122	209	58.4	98.6
U19	5	18	27.8	3.7
NTROI (U54)	3	3	100	3.8
Other U54	10	19	52.6	13.0
U56	4	40	10.0	3.1

*P01s and SPOREs are multi-component awards that typically include both research projects & core facilities.

Portfolio Analysis: Individual Research, Small Business & Intramural Awards

Funding Mechanism	Translational Awards	Total Active Awards	% Translational	TR Award Funding in FY04 (\$M)
R01	1,161	4,450	26.1%	\$447.0
R03	150	320	46.9	8.1
R21	288	599	48.1	43.8
R33	62	121	51.2	24.2
R37	11	74	14.9	6.6
R41	28	42	66.7	4.7
R42	12	19	63.2	3.8
R43	87	246	35.4	13.3
R44	102	176	58.0	39.4
Z01	257	630	40.8	164.4
Totals*	2,789	7,933	35.2	1,330.4

*"Totals" show amounts for all Program and Cooperative Awards, Developmental Program Projects, Career Development Awards, Individual Research Awards, Small Business Awards, and Intramural Awards, & it excludes the amounts for the Infrastructure Mechanisms.

Portfolio Analysis: Drug Development Programs & Infrastructure Mechanisms

Award Category	Translational Awards	Total Active Awards	% Translational	TR Award Funding in FY04 (\$M)
DDG	18	18	100%	\$11.1
RAID	45	45	100	16.3
RAPID	19	19	100	3.1

Award Category	Translational Awards	Total Active Awards	% Translational	TR Award Funding in FY04 (\$M)
P30*	54	61	88.5%	\$212.5
R24	8	43	18.6	1.5
U24	8	14	57.1	6.0
Extramural Cores (P01, P30, P50)	1,165	1,364	85.4	N/A

*Only Comprehensive and Clinical Cancer Centers were included here, not the Basic Cancer Centers.

Portfolio Analysis: Career Development Awards

Funding Mechanism	Translational Awards	Total Active Awards	% Translational	TR Award Funding in FY04 (\$M)
K01	14	116	12.1%	\$1.9
K05	1	19	5.3	0.1
K07	37	93	39.8	4.8
K08	21	139	15.1	2.5
K12	21	21	100	8.8
K22	13	42	31.0	1.4
K23	55	64	85.9	6.8
K24	25	34	73.5	2.2

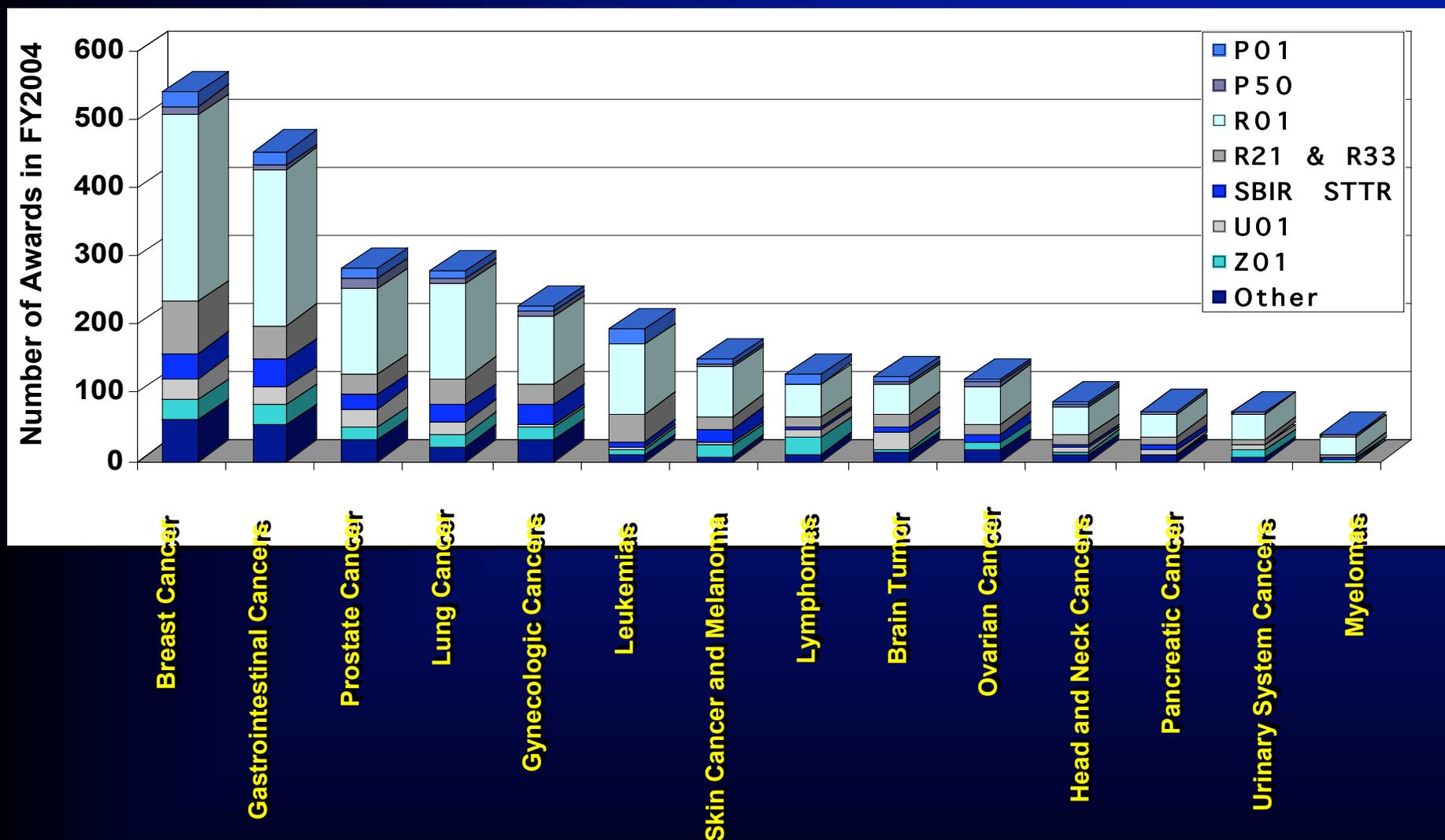
Portfolio Analysis: Clinical Trials

Trial Category	Translational Trials	Total Trials	\$ Millions in FY04
Phase I Clinical Trials	356	356	N/A*
Phase I/ Phase II Clinical Trials	155	155	N/A
Phase II Clinical Trials	855	855	N/A
Correlative Studies in Phase III Clinical Trials	221	221	N/A

*Funding support for clinical trials and correlative studies of clinical trials are included in other funding mechanisms, such as the U10, P01, P30, and SPORE program, as well as through investigator-initiated awards.

Total Number of Translational Awards in FY04

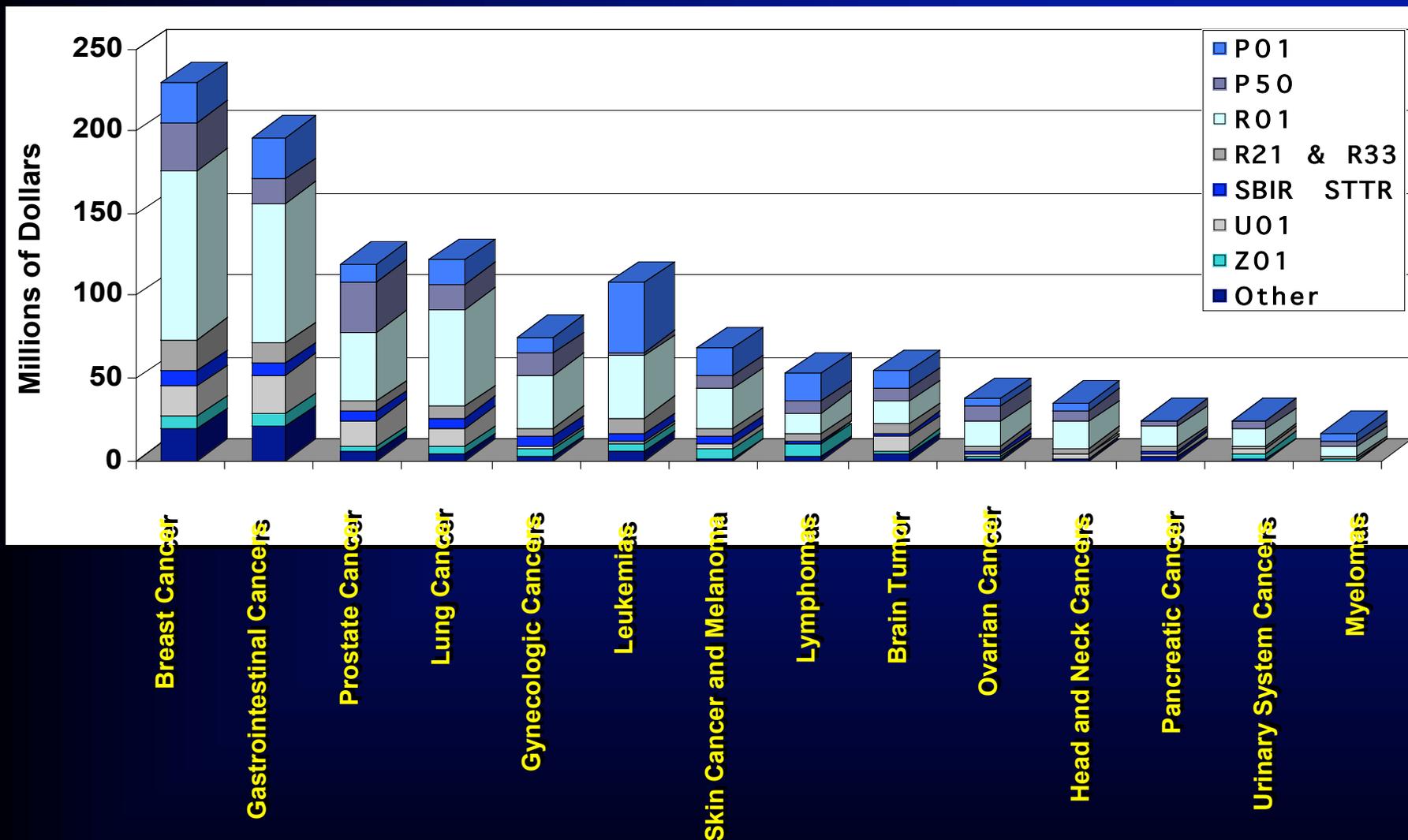
(>= 25% Relevant to these Disease Sites)



“Other” includes P20, P30, R03, R24, R37, U19, U24, U54, and U56 awards. K-series awards and U10 awards are not included.

Total FY04 Spending for Translational Awards

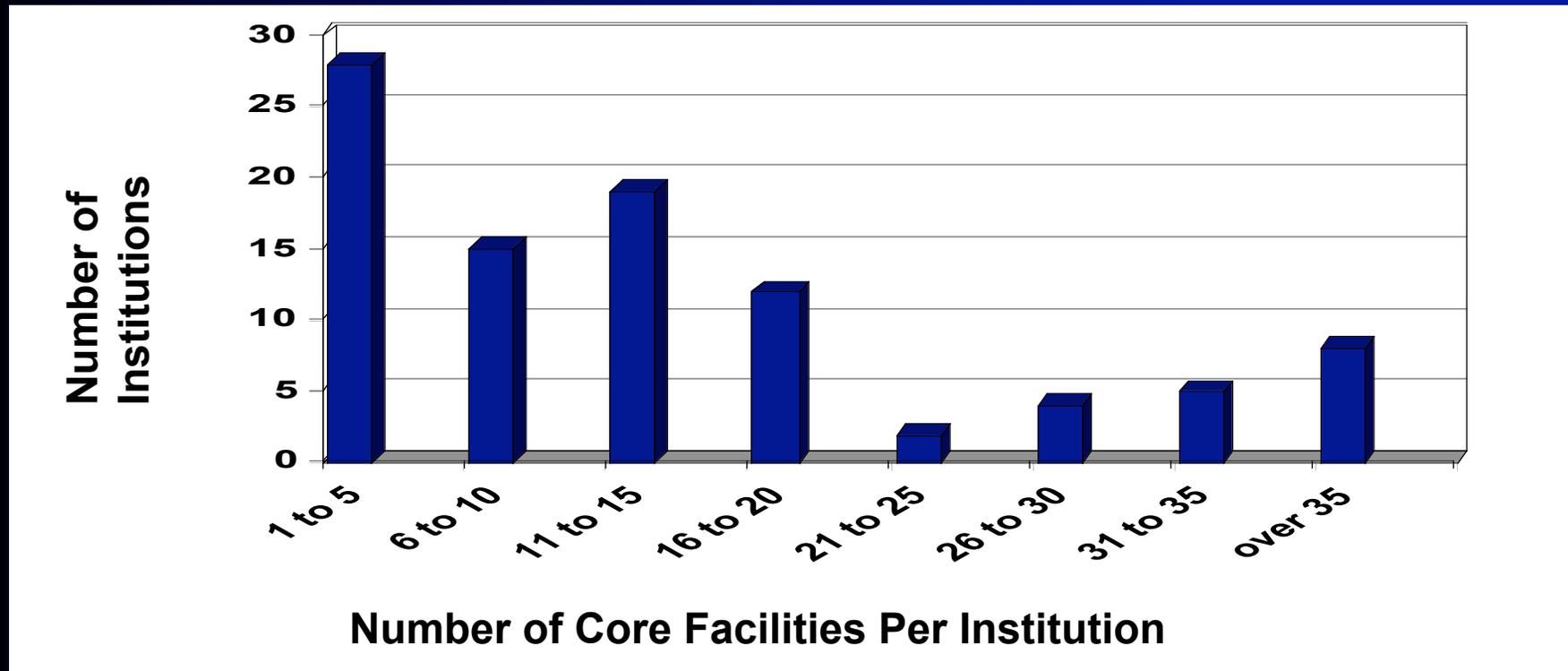
(>= 25% Relevant to these Disease Sites)



"Other" includes P20, P30, R03, R24, R37, U19, U24, U54, and U56 awards. K-series awards and U10 awards are not included.

Extramural Core Facilities Sponsored Through SPORE, P01, & P30 Mechanisms

Frequency Distribution

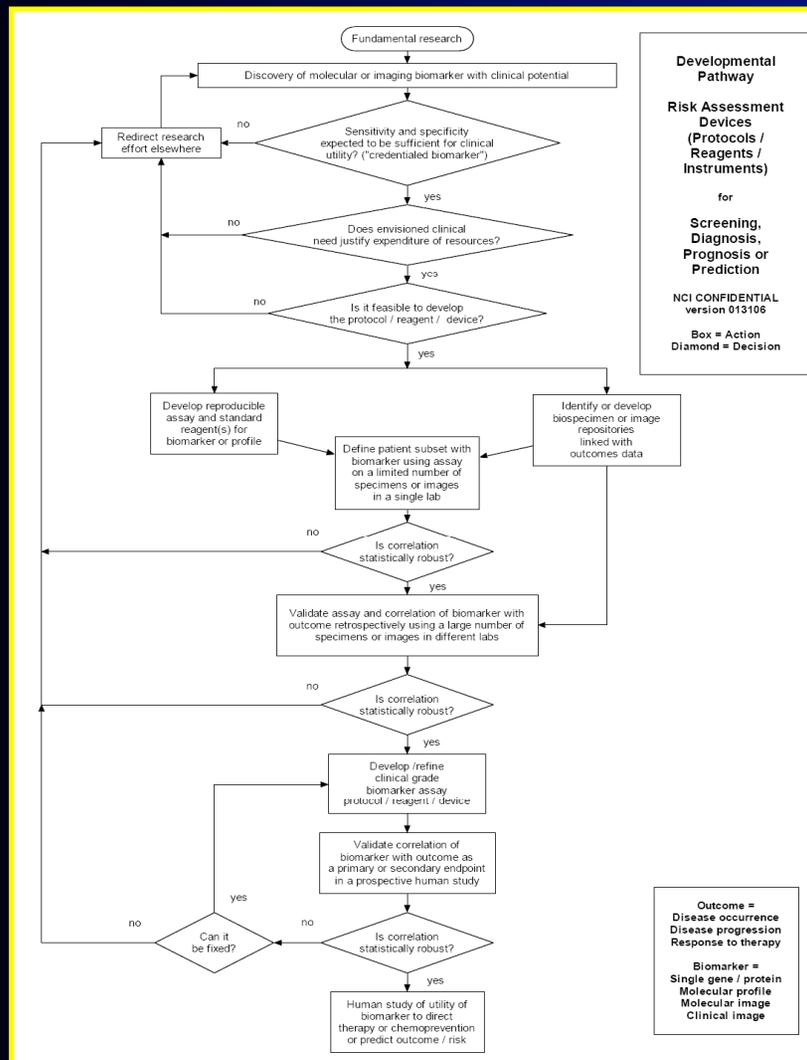


- Number of Core facilities includes all Basic, Clinical, & Comprehensive Cancer Center (P30) Core facilities, and all SPORE & P01 Core facilities identified from the SPORE website, CRISP database, and abstracts.

Portfolio Analysis: Key Findings

- Awards are not adequately categorized to provide meaningful, detailed quantitative assessments of translational content
- TR is funded by most NCI Divisions, Offices & Centers
- TR is funded by a range of mechanisms – individual, collaborative, & facilitated
- The majority of TR awards are to NCI-designated Cancer Centers

The Challenge of Early Translation



• How can we best assure that

- The most promising concepts enter the developmental pathway?
- Concepts that enter advance to the clinic or to productive failure?
- Progress is as rapid, efficient & effective as possible?

Draft Initiatives

- A. Coordinated Management - 4
- B. Tailored Funding Mechanisms - 5
- C. Operational Effectiveness - 8

TRWG - Upcoming Activities

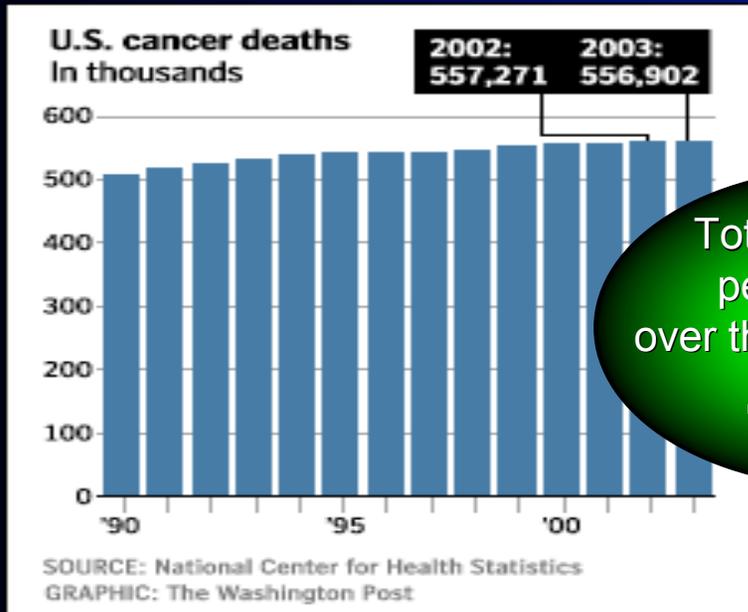
- **Invite public comment via web on draft recommendations**
 - October 13 – November 3, 2006 (www.cancer.gov/trwg)
- **Receive additional input from interested communities**
 - ASCO Translational Research Task Force
 - SPORE Directors
 - Cancer Center Directors
 - NCI Town Hall discussion
- **Finalize initiatives, implementation plans & report**
 - November 27 & 28, 2006
 - January 17 & 18, 2007
- **Present final model, recommendations & implementation plan to NCAB**
 - February 5-7, 2007

Drawing Inspiration from Pasteur

“To the individual who devotes his/her life to science nothing can give more happiness than when the results immediately find practical application. There are not two sciences. There is science and the application of science, and these two are linked as the fruit is to the tree.”

Louis Pasteur, 1822-95

CANCER TODAY



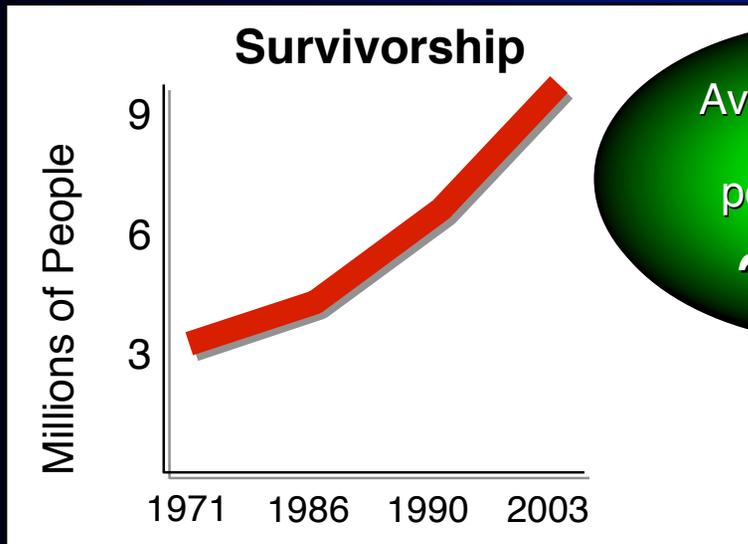
Total investment per American over the past 30 years:
~\$260

- For the first time annual cancer deaths in the United States have fallen

15 million survivors

Early detection and screening are more effective

- New targeted, minimally invasive treatments for cancer have multiplied



Average annual investment per American:
~\$8.60

New discoveries make it possible for the first time to "PERSONALIZE" cancer treatment

Thank You!